COCHRANE COLLABORATION HELPING UNRAVEL TANGLED WEB WOVEN BY INTERNATIONAL RESEARCH

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In Brief • En bref

Although there are sceptics and critics, the Cochrane Collaboration continues to grow exponentially. With centres in nine countries, its common goal is to create, maintain and disseminate systematic reviews of randomized controlled trials in an effort to bring clinicians the most current, accurate evidence about medical treatments available around the world. The future of the collaboration will depend largely on whether the methodology of their reviews can be shown to be valid and to produce consistently relevant and timely reviews.

Même s'il y a des sceptiques et des critiques, la collaboration Cochrane continue de prendre une croissance exponentielle. Comme il y a des centres dans neuf pays, son but commun est de créer, tenir et diffuser des revues systématiques d'études contrôlées randomisées afin de fournir aux cliniciens les données probantes les plus courantes et exactes au sujet de traitements médicaux disponibles dans le monde. L'avenir de la collaboration dépendra en grande partie de la question de savoir si l'on peut démontrer que la méthodologie des revues est valable et produit des revues toujours pertinentes et à en temps opportun.

When it comes to health care, everybody — medical professionals, policymakers and patients — wants to know what works and what doesn't. Every day doctors debate, implicitly or explicitly, whether new research findings are convincing enough to change the way they practise. The quality of research varies, and so much information is being produced that it is impossible for anyone to know and evaluate it all. Members of the Cochrane Collaboration believe they have begun to find an answer to this imbroglio, and if the growth that was evident at their third annual conference in Oslo last fall is any indicator, the world is beginning to take note.

The Cochrane Collaboration was established in England in 1992, under the leadership of Dr. Iain Chalmers, in response to a challenge from Archie Cochrane years earlier to organize a critical summary of all randomized controlled trials (RCTs). Cochrane, a physician and epidemiologist, argued that there will always be limits on health care resources so it is important to be sure that interventions being used are effective.

In the past 3 years the collaboration has witnessed phenomenal growth, with membership doubling every 6 months since its inception. There are now nine centres worldwide, including ones in Canada, the Netherlands, Denmark, Italy and Australia. There are three in the US, with plans to open new centres in the US, France, Spain, Germany and South Africa. Their common goal is to create, maintain and disseminate systematic reviews of RCTs.

A Cochrane review is based on an exhaustive search for all RCTs, published and unpublished, on a particular topic. This is followed by an analysis of these studies based on the principles behind evidence-based medicine. The final result from each study is usually transformed into an odds ratio; these are combined across studies into an overall "summary statistic." This mathematic synthesis of trial results constitutes a meta-analysis, a specialized form of systematic review. The Cochrane Collaboration logo is an example: it is based on a review of corticosteroids for threatened preterm delivery and the way these results and the overall summary statistic are presented.

ACCOMPLISHMENTS

Iain Chalmers and a host of colleagues responded to Cochrane's challenge by starting with research in obstetrics; the result was the Cochrane Database on Pregnancy and Childbirth. Despite initial resis-

Dr. Patricia Huston, CMAJ's associate editor-in-chief, attended the third Cochrane Colloquium in Oslo last year.

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tance to this approach and some of its conclusions, today few physicians would argue against the profound effect the database has had in transforming obstetric practice and research. With that database the gauntlet was dropped: there was no reason why this could not be done for all aspects of health care.

The Cochrane Collaboration has two goals: to discover where all results of all RCTs ever conducted are reported, and to summarize and disseminate this information in the form of systematic reviews. Pursuit of the former led to the first international clinical trial registry, while the latter led to the Cochrane Database of Systematic Reviews.

The International Trial Registry

During the 1995 Oslo conference Dr. Kay Dickerson, director of the Baltimore Cochrane Centre, and Carol Lefebvre, an information specialist with the United Kingdom Cochrane Centre, described their recent work with the National Library of Medicine (NLM). Their data showed that only half of the RCTs available in *Medline* are retrievable by routine searches because many trials are not properly "tagged." They also showed that *Medline* contains less than half of all published RCTs — this was discovered after members of Cochrane Collaborative Review Groups (see sidebar) found all these trials through exhaustive hand searching of journals.

This information led to an important change in NLM policy: based on citations supplied by the Baltimore Cochrane Centre, the NLM will retag all RCTs that had not been properly tagged and will set up a supplemental database to identify clinical trials in non-*Medline* journals. Pending the resolution of a few technical difficulties, this major contribution soon will be available to all.

The Cochrane Database of Systematic Reviews

The Cochrane Collaboration compiled its first database of systematic reviews in April 1995 and distributed its second volume in November. Described as a biannual electronic journal of systematic reviews, it is available on diskette (IBM or Macintosh) and CD-ROM.

The first volume was rather sparse but the current volume contains 65 reviews, mostly in internal medicine (cardiovascular problems, gastrointestinal disease, rheumatology) and obstetrics. This electronic journal also identifies reviews that are under way, either by title — more than 160 are noted — or by proposed methodology or protocol. A lot of useful information has been brought together in a scholarly and concise fashion, and is easily retrievable by a search strategy using author names or key words.

The Cochrane Database of Systematic Reviews (CDSR) includes two additional databases. One contains abstracts of systematic reviews of effectiveness that includes citations for about 800 non-Cochrane systematic reviews and abstracts for about 200 of them. The second is a smaller database of citations on the methodology for conducting systematic reviews.

The CDSR also includes the complete Cochrane Handbook, which contains information on how to form a review group and do systematic reviews and hand searches, as well as contact information for existing groups. (To order the CDSR see the CMA Publications catalogue or call CMA Membership Services, 800 663-7336.)

Problems

Although the Cochrane Collaboration has realized some significant accomplishments over the last 3 years, there have been growing pains. These could be described as outside criticisms and internal difficulties.

Overzealous pursuit

Those promoting the collaboration have been accused of being too dogmatic, of having a born-again fervour for their mission that makes them idealize RCT-related evidence. There is considerable speculation about reasons for this attitude.

Many participants, and especially the leaders, recount moving experiences that inspired them to become involved. In Oslo, for example, Iain Chalmers recounted why he had decided to take up Archie Cochrane's call: "I realized that I had killed babies because I had followed expert opinion rather than seeking out the evidence." Another physician described how thousands of Americans had died because of unnecessary antiarrhythmic medication, based on research that had not included appropriate endpoints.

There also was an altruistic aspect to the initial groundwork. There has not been a lot of academic recognition of systematic reviews, which were regarded as "secondary research." Similarly, funding for the reviews has been in much shorter supply than for primary research. When people work for little or no money in their spare time, undertaking clerical tasks such as hand searches of journals and receiving scant recognition for their work, observers may wonder if it is because Cochranites consider that they have some higher calling. Obviously, they believe in what they are doing.

RCT evidence isn't everything

A common criticism of Cochranites is that they give little credit to clinical experience. This is also linked with the notion that they are so focused on the evidence for treatment that they may not take enough

time to establish a correct diagnosis or to understand their patients' preferences. Dr. David Sackett, a founding father of evidence-based medicine who currently chairs the steering group for the Cochrane Collaboration, responds to this allegation by stating that the goal is to build upon good clinical skills and sound clinical experience. Ideally this is true, but critics sometimes feel there is an overreliance on hard data and perhaps an unrealistic expectation of the clinical applicability of RCTs. Many patients have multiple conditions or unique situations that place them in a "grey zone" in terms of the direct applicability of published medical research.

Because their work focuses on summarizing information from RCTs, collaborators have also been accused of "looking for the keys under the lamplight" and ignoring vast areas of medical information that have been made available through other research methods. Most Cochranites acknowledge that other areas of research offer useful information, but since the RCT is the most powerful research design it is a good place to start. Some review groups have gone even further and conducted reviews of observational studies.

Internal difficulties

Difficulties with communication and infrastructure are found in most rapidly growing organizations. Although the collaboration's reliance on electronic communication has allowed it to branch out quickly internationally, some members have felt inundated with information, yet uncertain about some very basic facts. For example, estimates of the number of Cochranites vary because there is not a complete membership registry.

Another difficulty is financial sustainability. The UK centre has fairly solid financial support, and the Canadian centre recently received a large grant from the Medical Research Council; others rely largely on "soft funding." The annual report identified 82 different sources of financial support for all the centres, so considerable effort is required simply to maintain financial viability.

Perhaps the most disquieting problem, however, concerned the methodology of systematic reviews. In Oslo, it was noted that differences in selection criteria — which articles should or should not be included in a review? — can totally alter a review's conclusion. Many quality-assessment forms used to evaluate which RCTs should be included in a review have not been validated. The conclusions of some systematic reviews (not necessarily Cochrane reviews) have been shown to disagree with the results of more recent large clinical trials. New, complex and more expensive methodologies are being promoted, such as reviews based on individual patient data in which reviewers must go back to the study authors to obtain the original data.

It is hard to tell whether these dif-

Organization of the Cochrane Collaboration

The activities of the Cochrane Collaboration are organized around Cochrane Centres, which keep track of researchers affiliated with the centres and support their Cochrane-related activities. Each centre is responsible for obtaining and maintaining its own funding, and carries out some activities that contribute to the collaboration as a whole. The United Kingdom Centre, for example, has been developing software, such as RevMan, which will assist in the preparation of systematic reviews. The Canadian Cochrane Centre has been working on Internet communications.

The major activity is the completion of systematic reviews, which are produced by collaborative review groups. Cochrane reviews are written by a team with as few as 3 or 4 members, or as many as 40. They can come from anywhere, although each review group is supported by one centre. Canada has four registered review groups that are studying inflammatory bowel disease, musculoskeletal problems, subfertility and neonatal issues. Each group has a facilitator, usually a physician, and an administrator. Not only does each group prepare reviews for the Cochrane Database of Systematic Reviews but also they commit to updating these reviews as new information arrives.

There are also Cochrane fields, which provide an opportunity for those whose interests cross different collaborative review groups to be represented within the collaboration. Examples are an interest in a particular age group, a particular medical specialty or a class of therapy.

Like the review groups, each field is affiliated with a single centre. Conceptually, the review groups provide a type of "vertical" or in-depth study function, while the fields provide a "horizontal" or liaison function. Currently there is only one registered field, in the area of primary care, which is based in Australia. Many others have been proposed and will likely be registered in the next year. A field for patients, the Consumer Network, was proposed at the second Cochrane Colloquium and approved at last year's meeting in Oslo.

Finally, there are methods groups, whose members share a common interest in some aspect of the methodology of systematic reviews. A statistics group based in England was one of the first methods groups; others, such as groups for quality assessment and peer review of systematic reviews, are being organized.

ficulties are simply the "growing pains" of a relatively new discipline or whether systematic reviews may not be the ultimate answer to medical queries.

THE FUTURE

Members of the Cochrane Collaboration are becoming increasingly aware that their zeal needs to be moderated, that RCTs are not the answer to all problems and that much work lies ahead. However, the need remains to summarize critically information on medical research.

In its short lifespan the collaboration has gained worldwide recognition. Increasingly, research funding is being provided for systematic reviews and for developing and evaluating their methodology. Information gained from reviews is being used by health care professionals, policymakers and researchers. Its effect on policy and practice is difficult to gauge, but it certainly has contributed to the promotion of higher quality clinical trials.

The future of the Cochrane Collaboration is far from assured. It will depend to a large extent on whether the methodology of reviews can be shown empirically to be valid, as well as on the collaboration's ongoing productivity in producing relevant and timely reviews. For the moment, it remains a bold, noble and imperfect enterprise. ■

Conferences continued from page 1362

June 22–25, 1996: Canadian Ophthalmological Society Annual Meeting and Exhibition
Ottawa
Canadian Ophthalmological Society, 610–1525 Carling Ave., Ottawa ON K1Z 8R9; tel 613 729-6779, fax 613 729-7209

June 22–26, 1996: Canadian Paediatric Society 73rd Annual Meeting
Saskatoon
Canadian Paediatric Society, 401 Smyth Rd., Ottawa ON K1H 8L1; tel 613 738-3900, fax 613 737-2794

June 23–29, 1996: International Society of Technology Assessment in Health Care (ISTAHC) 12th Annual Meeting
San Francisco
ISTAHC '96, KREBS Convention Management Services, 200–555 DeHaro St., San Francisco CA 94107

June 25–29, 1996: Canadian Congress of Neurological Sciences 31st Meeting
London, Ont.
Susan M. Markey, Canadian Congress of Neurological Sciences, 810–906 12th Ave. SW, Calgary AB T2R 1K7; tel 403 229-9544, fax 403 229-1661

June 26–29, 1996: 10th International Computer Assisted Radiology Symposium and Exhibition (in collaboration with the Société française de radiologie et d'imagerie médicale, the International Society of Computer Aided Surgery and the International Association of Dento-Maxillo-Facial Radiology)
Paris, France
CAR '96, Prof. Heinz U. Lemke, c/o Technische Universität Berlin, Institut für Technische Informatik, Sekr. CG FR 3-3, Franklinstrasse 28-29, D-10587 Berlin, Germany; tel 49 0 7742-7746, fax 49 0 7742-4391

June 26–29, 1996: 22nd Canadian Medical and Biological Engineering Conference (CMBEC): Biotechnology and Funding Healthcare
Charlottetown
CMBEC Secretariat, c/o National Research Council, Rm 393, Bldg M-55, Ottawa ON K1A 0R8; tel 613 993-1686, fax 613 954-2216, sally.chapman@nrc.ca

July 6, 1996: HIV Prevention Works (satellite symposium of the 11th International Conference on AIDS, presented in collaboration with the National AIDS Strategy of Health Canada, the Joint United Nations Programme on HIV/AIDS and the US Centers for Disease Control and Prevention)
Vancouver
Canadian Public Health Association, 400–1565 Carling Ave., Ottawa ON K1Z 8R1; tel 613 725-3769, fax 613 725-9826

Le 6 juill. 1996 : La prévention du VIH, ça marche (symposium satellite de la 11e Conférence internationale sur le SIDA, en collaboration avec la Stratégie nationale sur le SIDA de Santé Canada, le Programme commun des Nations Unies sur le VIH/SIDA et les Centers for Disease Control and Prevention américains)
Vancouver
Association canadienne de santé publique, 400–1565, ave. Carling, Ottawa ON K1Z 8R1; tél 613 725-3769, fax 613 725-9826

Oct. 6–9, 1996: Carcinogenesis from Environmental Pollution: Assessment of Human Risk and Strategies for Prevention (joint conference of the American Association for Cancer Research and the International Agency for Research on Cancer with the collaboration of the Hungarian Cancer Society)
Budapest, Hungary
Special Conference Registration, American Association for Cancer Research, Suite 816, Public Ledger Building, 150 S Independence Mall W, Philadelphia PA 19106-3483; tel 215 440-9300, fax 215 440-9313

Oct. 13–16, 1996: Society for Medical Decision Making 18th Annual Scientific Meeting
Toronto
Society for Medical Decision Making, htl@ices.on.ca, amona@acadvm1.uottawa.ca

Dec. 4–7, 1996: 1st World Congress of Pediatric Infectious Diseases (sponsored by the World Society of Pediatric Infectious Diseases)
Acapulco, Mexico
Dr. Napoleon Gonzalez Saldaña, Instituto Nacional de Pediatria, CP 04530, PO Box 101-53, Mexico, DF; tel 525 606-0002, ext. 367; fax 525 606-6856

Dec. 4–7, 1996: 3rd International Conference on Long-term Care Case Management — Bridging the Many Worlds of Case Management
San Diego
American Society on Aging, 511–833 Market St., San Francisco CA 94103-1824; tel 415 974-9600, fax 415 974-0300

Feb. 18–22, 1997: 10th Biennial International Symposium on Hypoxia and Mountain Medicine — Women at Altitude
Lake Louise, Alta.
Abstract deadline: Nov. 1, 1996
Sharon Studd, conference coordinator, Continuing Education, Faculty of Health Sciences, Rm. 1M7, 1200 Main St. W, Hamilton ON L8N 3Z5; tel 905 525-9140, ext. 22671, fax 905 572-7099; studd@fhs.csu.mcmaster.ca

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